Drug and Biologic Coverage Policy

Effective Date ........................................ 2/1/2020
Next Review Date ..................................... 2/1/2021
Coverage Policy Number ............................... 1611

Filgrastim

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Related Coverage Resources

Pegfilgrastim – (1320)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Granulocyte Colony Stimulating Factors (G-CSF) include the following:

<table>
<thead>
<tr>
<th>Preferred Brand</th>
<th>Non-Preferred Brand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granix® (tbo-filgrastim)</td>
<td>Neupogen® (filgrastim)</td>
</tr>
<tr>
<td>Zarxio® (filgrastim-sndz)</td>
<td>Nivestym™ (filgrastim-aafi)</td>
</tr>
</tbody>
</table>

Cigna covers filgrastim (Neupogen, Nivestym) as medically necessary when ANY of the following is met:

- Documented failure or inadequate response, intolerance, or inability to use (for example: dose less than 180 mcg tbo-filgrastim (Granix) AND filgrastim-sndz (Zarxio))
- Documentation of continuation of therapy to complete current cycle of myelosuppressive chemotherapy
- Use in hematopoietic cell transplant

Initial and reauthorization is up to 1 month.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.
Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

### FDA Approved Indications

#### FDA Approved Indication

<table>
<thead>
<tr>
<th>Product</th>
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<tr>
<td>Granix (tbo-filgrastim)</td>
<td>Granix is indicated to reduce the duration of severe neutropenia in adult and pediatric patients 1 month and older with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.</td>
</tr>
</tbody>
</table>
| Neupogen (filgrastim) | **Patients with Cancer Receiving Myelosuppressive Chemotherapy**<br>Neupogen is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever.  
**Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**<br>Neupogen is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).  
**Patients with Cancer Undergoing Bone Marrow Transplantation**<br>Neupogen is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.  
**Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**<br>Neupogen is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.  
**Patients with Severe Chronic Neutropenia**<br>Neupogen is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.  
**Patients Acutely Exposed to Myelosuppressive Doses of Radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)**<br>Neupogen is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation. |
| Nivestym (filgrastim-aafi) | **Patients with Cancer Receiving Myelosuppressive Chemotherapy**<br>Nivestym is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever.  
**Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**<br>Nivestym is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).  
**Patients with Cancer Undergoing Bone Marrow Transplantation**<br>Nivestym is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation. |
**Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**
Nivestym is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

**Patients with Severe Chronic Neutropenia**
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### Recommended Dosing

**FDA Recommended Dosing**

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<th><strong>FDA Recommended Dosing</strong></th>
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| **Granix** (tbo-filgrastim) | The recommended dose of Granix is 5 mcg/kg per day administered as a subcutaneous injection. Administer the first dose of Granix no earlier than 24 hours following myelosuppressive chemotherapy. Do not administer Granix within 24 hours prior to chemotherapy.  

Daily dosing with Granix should continue until the expected neutrophil nadir is passed and the neutrophil count has recovered to the normal range. Monitor complete blood count (CBC) prior to chemotherapy and twice per week until recovery. |

| **Neupogen** (filgrastim) | **Dosage in Patients with Cancer Receiving Myelosuppressive Chemotherapy or Induction and/or Consolidation Chemotherapy for AML**  
The recommended starting dosage of Neupogen is 5 mcg/kg/day, administered as a single daily injection by subcutaneous injection, by short intravenous infusion (15 to 30 minutes), or by continuous intravenous infusion. Obtain a complete blood count (CBC) and platelet count before instituting Neupogen therapy and monitor twice weekly during therapy. Consider dose escalation in increments of 5 mcg/kg for each chemotherapy cycle. |

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according to the duration and severity of the absolute neutrophil count (ANC) nadir. Recommend stopping Neupogen if the ANC increases beyond 10,000/mm³.

Administer Neupogen at least 24 hours after cytotoxic chemotherapy. Do not administer Neupogen within the 24-hour period prior to chemotherapy. A transient increase in neutrophil count is typically seen 1 to 2 days after initiation of Neupogen therapy. Therefore, to ensure a sustained therapeutic response, administer Neupogen daily for up to 2 weeks or until the ANC has reached 10,000/mm³ following the expected chemotherapy-induced neutrophil nadir. The duration of Neupogen therapy needed to attenuate chemotherapy-induced neutropenia may be dependent on the myelosuppressive potential of the chemotherapy regimen employed.

**Dosage in Patients with Cancer Undergoing Bone Marrow Transplantation**

The recommended dosage of Neupogen following bone marrow transplantation (BMT) is 10 mcg/kg/day given as an intravenous infusion no longer than 24 hours. Administer the first dose of Neupogen at least 24 hours after cytotoxic chemotherapy and at least 24 hours after bone marrow infusion. Monitor CBCs and platelet counts frequently following marrow transplantation.

During the period of neutrophil recovery, titrate the daily dosage of Neupogen against the neutrophil response (see Table 1).

**Table 1: Recommended Dosage Adjustments During Neutrophil Recovery in Patients with Cancer Following BMT**

<table>
<thead>
<tr>
<th>Absolute Neutrophil Count</th>
<th>Neupogen Dosage Adjustment</th>
</tr>
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</table>
| When ANC greater than 1000/mm³ for 3 consecutive days | Reduce to 5 mcg/kg/day
| Then, if ANC remains greater than 1000/mm³ for 3 more consecutive days | Discontinue Neupogen
| Then, if ANC decreases to less than 1000/mm³ | Resume at 5 mcg/kg/day

*If ANC decreases to less than 1000/mm³ at any time during the 5 mcg/kg/day administration, increase Neupogen to 10 mcg/kg/day, and then follow the above steps.*

**Dosage in Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**

The recommended dosage of Neupogen for the mobilization of autologous peripheral blood progenitor cells (PBPC) is 10 mcg/kg/day given by subcutaneous injection. Administer Neupogen for at least 4 days before the first leukapheresis procedure and continue until the last leukapheresis. Although the optimal duration of Neupogen administration and leukapheresis schedule have not been established, administration of Neupogen for 6 to 7 days with leukaphereses on days 5, 6, and 7 was found to be safe and effective. Monitor neutrophil counts after 4 days of Neupogen, and discontinue Neupogen if the white blood cell (WBC) count rises to greater than 100,000/mm³.

**Dosage in Patients with Severe Chronic Neutropenia**

Prior to starting Neupogen in patients with suspected chronic neutropenia, confirm the diagnosis of severe chronic neutropenia (SCN) by evaluating serial CBCs with differential and platelet counts, and evaluating bone marrow morphology and karyotype. The use of Neupogen prior to confirmation of a correct diagnosis of SCN may impair diagnostic efforts and may thus impair or delay evaluation and treatment of an underlying condition, other than SCN, causing the neutropenia.

The recommended starting dosage in patients with Congenital Neutropenia is 6 mcg/kg as a twice daily subcutaneous injection and the recommended starting dosage in patients with Idiopathic or Cyclic Neutropenia is 5 mcg/kg as a single daily subcutaneous injection.
### Dosage Adjustments in Patients with Severe Chronic Neutropenia

Chronic daily administration is required to maintain clinical benefit. Individualize the dosage based on the patient’s clinical course as well as ANC. In the SCN post-marketing surveillance study, the reported median daily doses of Neupogen were: 6 mcg/kg (congenital neutropenia), 2.1 mcg/kg (cyclic neutropenia), and 1.2 mcg/kg (idiopathic neutropenia). In rare instances, patients with congenital neutropenia have required doses of Neupogen greater than or equal to 100 mcg/kg/day.

**Monitor CBCs for Dosage Adjustments**

During the initial 4 weeks of Neupogen therapy and during the 2 weeks following any dosage adjustment, monitor CBCs with differential and platelet counts. Once a patient is clinically stable, monitor CBCs with differential and platelet counts monthly during the first year of treatment. Thereafter, if the patient is clinically stable, less frequent routine monitoring is recommended.

### Dosage in Patients Acutely Exposed to Myelosuppressive Doses of Radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)

The recommended dose of Neupogen is 10 mcg/kg as a single daily subcutaneous injection for patients exposed to myelosuppressive doses of radiation. Administer Neupogen as soon as possible after suspected or confirmed exposure to radiation doses greater than 2 gray (Gy).

Estimate a patient’s absorbed radiation dose (i.e., level of radiation exposure) based on information from public health authorities, biodosimetry if available, or clinical findings such as time to onset of vomiting or lymphocyte depletion kinetics.

Obtain a baseline CBC and then serial CBCs approximately every third day until the ANC remains greater than 1,000/mm³ for 3 consecutive CBCs. Do not delay administration of Neupogen if a CBC is not readily available.

Continue administration of Neupogen until the ANC remains greater than 1,000/mm³ for 3 consecutive CBCs or exceeds 10,000/mm³ after a radiation-induced nadir.

### Nivestym (filgrastim-aafi)

#### Dosage in Patients with Cancer Receiving Myelosuppressive Chemotherapy or Induction and/or Consolidation Chemotherapy for AML

The recommended starting dosage of Nivestym is 5 mcg/kg/day, administered as a single daily injection by subcutaneous injection, by short intravenous infusion (15 to 30 minutes), or by continuous intravenous infusion. Obtain a complete blood count (CBC) and platelet count before instituting Nivestym therapy and monitor twice weekly during therapy. Consider dose escalation in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the absolute neutrophil count (ANC) nadir. Recommend stopping Nivestym if the ANC increases beyond 10,000/mm³.

Administer Nivestym at least 24 hours after cytotoxic chemotherapy. Do not administer Nivestym within the 24-hour period prior to chemotherapy. A transient increase in neutrophil count is typically seen 1 to 2 days after initiation of Nivestym therapy. Therefore, to ensure a sustained therapeutic response, administer Nivestym daily for up to 2 weeks or until the ANC has reached 10,000/mm³ following the expected chemotherapy-induced neutrophil nadir. The duration of Nivestym therapy needed to attenuate chemotherapy-induced neutropenia may be dependent on the myelosuppressive potential of the chemotherapy regimen employed.

#### Dosage in Patients with Cancer Undergoing Bone Marrow Transplantation

The recommended dosage of Nivestym following bone marrow transplantation (BMT) is 10 mcg/kg/day given as an intravenous infusion no longer than 24 hours. Administer the first dose of Nivestym at least 24 hours after cytotoxic chemotherapy and at least 24 hours after
bone marrow infusion. Monitor CBCs and platelet counts frequently following marrow transplantation.

During the period of neutrophil recovery, titrate the daily dosage of Nivestym against the neutrophil response (see Table 1).

<table>
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<tr>
<th>Absolute Neutrophil Count</th>
<th>Nivestym Dosage Adjustment</th>
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| When ANC greater than 1000/mm³ for 3 consecutive days | Reduce to 5 mcg/kg/day
| Then, if ANC remains greater than 1000/mm³ for 3 more consecutive days | Discontinue Nivestym |
| Then, if ANC decreases to less than 1000/mm³ | Resume at 5 mcg/kg/day |

a If ANC decreases to less than 1000/mm³ at any time during the 5 mcg/kg/day administration, increase Nivestym to 10 mcg/kg/day, and then follow the above steps.

**Dosage in Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**
The recommended dosage of Nivestym for the mobilization of autologous peripheral blood progenitor cells (PBPC) is 10 mcg/kg/day given by subcutaneous injection. Administer Nivestym for at least 4 days before the first leukapheresis procedure and continue until the last leukapheresis. Although the optimal duration of Nivestym administration and leukapheresis schedule have not been established, administration of filgrastim for 6 to 7 days with leukaphereses on days 5, 6, and 7 was found to be safe and effective. Monitor neutrophil counts after 4 days of Nivestym, and discontinue Nivestym if the white blood cell (WBC) count rises to greater than 100,000/mm³.

**Dosage in Patients with Severe Chronic Neutropenia**
Prior to starting Nivestym in patients with suspected chronic neutropenia, confirm the diagnosis of severe chronic neutropenia (SCN) by evaluating serial CBCs with differential and platelet counts, and evaluating bone marrow morphology and karyotype. The use of Nivestym prior to confirmation of a correct diagnosis of SCN may impair diagnostic efforts and may thus impair or delay evaluation and treatment of an underlying condition, other than SCN, causing the neutropenia.

The recommended starting dosage in patients with Congenital Neutropenia is 6 mcg/kg as a twice daily subcutaneous injection and the recommended starting dosage in patients with Idiopathic or Cyclic Neutropenia is 5 mcg/kg as a single daily subcutaneous injection.

**Dosage Adjustments in Patients with Severe Chronic Neutropenia**
Chronic daily administration is required to maintain clinical benefit. Individualize the dosage based on the patient’s clinical course as well as ANC. In the SCN post-marketing surveillance study, the reported median daily doses of filgrastim were: 6 mcg/kg (congenital neutropenia), 2.1 mcg/kg (cyclic neutropenia), and 1.2 mcg/kg (idiopathic neutropenia). In rare instances, patients with congenital neutropenia have required doses of filgrastim greater than or equal to 100 mcg/kg/day.

**Monitor CBCs for Dosage Adjustments**
During the initial 4 weeks of Nivestym therapy and during the 2 weeks following any dosage adjustment, monitor CBCs with differential and platelet counts. Once a patient is clinically stable, monitor CBCs with differential and platelet counts monthly during the first year of treatment. Thereafter, if the patient is clinically stable, less frequent routine monitoring is recommended.
**Dosage in Patients with Cancer Receiving Myelosuppressive Chemotherapy or Induction and/or Consolidation Chemotherapy for AML**

The recommended starting dosage of Zarxio is 5 mcg/kg/day, administered as a single daily injection by subcutaneous injection, by short intravenous infusion (15 to 30 minutes), or by continuous intravenous infusion. Obtain a complete blood count (CBC) and platelet count before instituting Zarxio therapy and monitor twice weekly during therapy. Consider dose escalation in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the absolute neutrophil count (ANC) nadir. Recommend stopping Zarxio if the ANC increases beyond 10,000/mm³.

Administer Zarxio at least 24 hours after cytotoxic chemotherapy. Do not administer Zarxio within the 24-hour period prior to chemotherapy. A transient increase in neutrophil count is typically seen 1 to 2 days after initiation of Zarxio therapy. Therefore, to ensure a sustained therapeutic response, administer Zarxio daily for up to 2 weeks or until the ANC has reached 10,000/mm³ following the expected chemotherapy-induced neutrophil nadir. The duration of Zarxio therapy needed to attenuate chemotherapy-induced neutropenia may be dependent on the myelosuppressive potential of the chemotherapy regimen employed.

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<td>Then, if ANC remains greater than 1000/mm³ for 3 more consecutive days</td>
<td>Discontinue Zarxio</td>
</tr>
<tr>
<td>Then, if ANC decreases to less than 1000/mm³</td>
<td>Resume at 5 mcg/kg/day</td>
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* If ANC decreases to less than 1000/mm³ at any time during the 5 mcg/kg/day administration, increase Zarxio to 10 mcg/kg/day, and then follow the above steps.

**Dosage in Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**

The recommended dosage of Zarxio for the mobilization of autologous peripheral blood progenitor cells (PBPC) is 10 mcg/kg/day given by subcutaneous injection. Administer Zarxio for at least 4 days before the first leukapheresis procedure and continue until the last leukapheresis. Although the optimal duration of Zarxio administration and leukapheresis schedule have not been established, administration of filgrastim for 6 to 7 days with leukaphereses on days 5, 6, and 7 was found to be safe and effective. Monitor neutrophil counts after 4 days of Zarxio, and discontinue Zarxio if the white blood cell (WBC) count rises to greater than 100,000/mm³.

**Dosage in Patients with Severe Chronic Neutropenia**

Prior to starting Zarxio in patients with suspected chronic neutropenia, confirm the diagnosis of severe chronic neutropenia (SCN) by evaluating serial CBCs with differential and platelet counts, and evaluating bone marrow morphology and karyotype. The use of Zarxio prior to confirmation of a correct diagnosis of SCN may impair diagnostic efforts and may thus...
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Monitor CBCs for Dosage Adjustments
During the initial 4 weeks of Zarxio therapy and during the 2 weeks following any dosage adjustment, monitor CBCs with differential and platelet counts. Once a patient is clinically stable, monitor CBCs with differential and platelet counts monthly during the first year of treatment. Thereafter, if the patient is clinically stable, less frequent routine monitoring is recommended.

Under Important Administration Instructions: Zarxio prefilled syringe with BD UltraSafe Passive™ Needle Guard is not designed to allow for direct administration of doses of less than 0.3 mL (180 mcg). The spring-mechanism of the needle guard apparatus affixed to the prefilled syringe interferes with the visibility of the graduation markings on the syringe barrel corresponding to 0.1 mL and 0.2 mL. The visibility of these markings is necessary to accurately measure doses of Zarxio less than 0.3 mL (180 mcg) for direct administration to patients. Thus, the direct administration to patients requiring doses of less than 0.3 mL (180 mcg) is not recommended due to the potential for dosing errors.

Drug Availability

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<tr>
<td>Granix</td>
<td>Supplied in single-dose vials containing 300 mcg/mL and 480 mcg/1.6 mL for injection and in single-dose prefilled syringes of 300 mcg/0.5 mL and 480 mcg/0.8 mL for injection.</td>
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<tr>
<td>Neupogen</td>
<td>Supplied in single-dose vials containing 300 mcg/mL and 480 mcg/1.6 mL for injection and in single-dose prefilled syringes of 300 mcg/0.5 mL and 480 mcg/0.8 mL for injection.</td>
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<tr>
<td>Nivestym</td>
<td>Supplied in single-dose vials containing 300 mcg/mL and 480 mcg/1.6 mL for injection and in single-dose prefilled syringes of 300 mcg/0.5 mL and 480 mcg/0.8 mL for injection.</td>
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<tr>
<td>Zarxio</td>
<td>Supplied as 300 mcg/0.5 mL and 480 mcg/0.8 mL for injection in single-dose prefilled syringes with BD UltraSafe Passive™ Needle Guard.</td>
</tr>
</tbody>
</table>

General Background

Pharmacology
Colony-stimulating factors are glycoproteins which act on hematopoietic cells by binding to specific cell surface receptors and stimulating proliferation, differentiation commitment, and some end-cell functional activation. Endogenous G-CSF is a lineage-specific colony-stimulating factor that is produced by monocytes, fibroblasts, and endothelial cells. G-CSF regulates the production of neutrophils within the bone marrow and affects neutrophil progenitor proliferation, differentiation, and selected end-cell functions (including enhanced phagocytic ability, priming of the cellular metabolism associated with respiratory burst, antibody-dependent killing, and the increased expression of some cell surface antigens). G-CSF is not species-specific and has been shown to have minimal direct in vivo or in vitro effects on the production or activity of hematopoietic cell types other than the neutrophil lineage.
**Professional Societies/Organizations**

**American Society for Blood and Marrow Transplantation (ASBMT)**
The ASBMT note that G-CSF is the standard used for peripheral blood progenitor cell (PBPC) mobilization in autologous and allogeneic hematopoietic cell transplantation. ASBMT also highlights that there is insufficient data to recommend use of biosimilar G-CSF for PBPC mobilization. (Duong, 2014)

**American Society of Clinical Oncology (ASCO)**
When the risk of FN is at least 20% or higher (based on myelotoxicity of specific agents used and patient and disease characteristics) and no equally efficacious and safe chemotherapy protocol exists that does not require CSF support, the use of prophylactic CSFs is appropriate. This primary prophylaxis should be initiated with the first cycle of chemotherapy and continue throughout the protocol. If a patient experiences a treatment cycle delay or a dose reduction, which jeopardizes clinical outcomes, due to a neutropenic episode, secondary prophylaxis is warranted. Alternatively, a dose reduction or therapy delay may be in order. The guidelines suggest that dose-dense protocols that require CSF support should be administered as part of a clinical trial or if there is strong evidence of efficacy. In the case of exposure to lethal doses of total-body radiotherapy, not at a level high enough to cause death, the recommendation is timely administration of CSFs. The committee did not address CSF use in adults with acute myeloid leukemia or myelodysplastic syndromes. The organization states that pegfilgrastim, filgrastim, tbo-filgrastim and filgrastim-sndz, and future biosimilars, are options for the prevention of treatment related FN, and the decision of which agent to use should be guided by convenience, cost and the clinical facts. (Smith, 2015)

**National Comprehensive Cancer Network (NCCN)**
The NCCN provides recommendations for the use of myeloid growth factors. The guidelines advocate continuing the same G-CSF throughout treatment. Filgrastim, filgrastim-sndz, and tbo-filgrastim are all recommended for prophylactic use for febrile neutropenia in individuals with solid tumors and non-myeloid malignancies at a high or intermediate risk. For individuals presenting with febrile neutropenia who were not on prophylactic G-CSF and have risk factors for an infection-associated complication, NCCN recommends myeloid growth factors with a notation that tbo-filgrastim and pegfilgrastim have only been evaluated for prophylactic use. In addition, NCCN provides recommendations for the use of filgrastim, filgrastim-sndz, and tbo-filgrastim for the mobilization of hematopoietic progenitor cells in the autologous setting. Filgrastim is listed as preferred with filgrastim-sndz and tbo-filgrastim as recommended for allogenic hematopoietic cell donors. (NCCN, 2017)

**Clinical Efficacy**
- **Granix (tbo-filgrastim)**
  Tbo-filgrastim (Granix) demonstrated superiority to placebo and equivalence to filgrastim (Neupogen) in terms of mean duration of severe neutropenia in breast cancer patients receiving docetaxel/doxorubicin in cycle 1. (delGiglio, 2008) A meta-analysis of 3 trials (including delGiglio et al) which included patients with breast cancer, lung cancer, and non-Hodgkin’s lymphoma was conducted to compare tbo-filgrastim (Granix) and filgrastim (Neupogen). The authors concluded that XM02 (tbo-filgrastim or Granix) was non-inferior to filgrastim for the incidence of febrile neutropenia regardless of the chemotherapy regimen. (Engert, 2009) The safety and effectiveness of Granix in pediatric patients have not been established.

- **Zarxio (filgrastim-sndz)**
  A randomized, double-blind, multicenter trial compared filgrastim-sndz (Zarxio) to the reference product, filgrastim (Neupogen) in 218 patients with breast cancer receiving chemotherapy with docetaxel/doxorubicin. Patients either remained on the same product throughout chemotherapy cycles or alternated products. Zarxio was non-inferior to Neupogen in terms of duration of severe neutropenia during cycle 1. Alternating products did not yield any differences in safety or efficacy. (Blackwell, 2015)

**Coding/ Billing Information**

**Note:**
1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.
Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J1442</td>
<td>Injection, filgrastim (g-csf), excludes biosimilars, 1 microgram</td>
</tr>
<tr>
<td>Q5110</td>
<td>Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 microgram</td>
</tr>
</tbody>
</table>

References

2. del Giglio A, Eniu A, Ganea-Motan, et al. XM02 is superior to placebo and equivalent to Neupogen in reducing the duration of severe neutropenia and the incidence of febrile neutropenia in cycle 1 in breast cancer patients receiving docetaxel/doxorubicin chemotherapy. BMC Cancer 2008; 8: 332.
11. Nivestym injection for subcutaneous or intravenous use [product information]. Lake Forest, IL: Hospira/Pfizer; July 2018.